REMARKS

The Amendments

The present claim set includes three independent claims, 130, 151 and 162, which derive from the subject matter of cancelled claims 91, 90 and 120, respectively. Specifically, present claim 130 covers the aspect of the cancelled independent claim 91, although further reciting "administration by non-oral means." New claim 151 includes the subject matter of cancelled dependent claim 90 that was directed to a composition wherein the NET derivative and the androgen were formulated in separate formulations. That is to say that this subject matter relates to a kit comprising separate formulations of the NET derivative and the androgen as cited in new claim 151. Finally, the subject matter of cancelled claim 120 is now included in present claim 162, except that the administration of an androgen is not incorporated as an essential feature but cited in dependent claim 171.

Though not limited thereto, support for each of the claims in the present claim set is provided, for example, as shown in the following table:

CLAIM NO:	BASIS
130:	Cancelled independent claim 91. Support for incorporating the element "administration by non-oral means" is found in the Specification on page 11, line 19. Support for incorporating the element "the effective amount corresponds to that upon administration of said norethisterone derivative the effective levels in the circulation are sustained for not less than 4 weeks" is found on page 9, lines 31-35 of the Specification. It is to be understood that the wording "effective levels in the circulation are sustained for not less than 4 weeks" is meant to express that upon each administering of the hormone, the effective levels in the circulation are maintained until the subsequent administration of the hormone takes place.
131:	Corresponds to cancelled claim 92. Supported by the text on page 9, lines 31-35, of the Specification. Further amended so as to include the wording of claim 130.

CLAIM NO:	BASIS
132:	Corresponds to cancelled claim 93. Supported by the text on page 9, lines 31-35, of the Specification. Further amended so as to include the wording of claim 130.
133:	Corresponds to cancelled claim 94. Supported by the text on page 10, lines 24-27, of the Specification.
134:	Corresponds to cancelled claim 95. Supported by the text on page 10, lines 24-27, of the Specification.
135:	Corresponds to cancelled claim 97. Supported by the text on page 9, lines 7-8, of the Specification.
136:	Corresponds to cancelled claim 101. Support is found in the text on page 4, lines 23-25, of the Specification.
137:	Corresponds to cancelled claim 102. Support is found in the text on page 8, lines 7-10, of the Specification.
138:	Corresponds to cancelled claim 103. Support is found in the text on page 8, lines 7-10, of the Specification.
139:	Corresponds to cancelled claim 104. Support is found in the text on page 8, line 12, of the Specification.
140:	Support is found in the text on page 8, line 14.
141:	Support is found in the text on page 8, lines 14-17.
142:	Support is found in the text on page 8, line 18.
143:	Support is found in the text on page 10, lines 13-15.
144:	Support is found in the text on page 10. lines 13-15.
145:	Support is found in the text on page 10, lines 31-33.
146:	Support is found in the text on page 10, lines 17-20.
147:	Support is found in the text on page 10, lines 17-20.
148:	Support is found in the text on page 11, lines 19-24.
149:	Support is found in the text on page 17, lines 16-18.
150:	Support is found in the text on page 17, lines 16-18.
151:	Support for claiming a composition in a unit dosage form is found in the text on page 12, lines 9-10, of the Specification. Support for incorporating the expression "wherein said norethisterone derivative and said androgen is in separate dosage units" is found in the text on page 16, lines 27-28. Support for the further wording is as in claim 130.

CLAIM NO:	BASIS
152:	Support is found as in present claim 131.
153:	Support is found as in present claim 133.
154:	Support is found as in present claim 135.
155-158:	The subject matter of claims 155 to 158 is similar to that cited in present claims 140-145.
159-161:	The subject matter of claims 159 to 161 is similar to that cited in present claims 148 to 149, respectively.
162:	Support is found in the text on page 17, lines 20-24, of the Specification and further as cited for present claim 130.
163-170:	The subject matter of claims 163 to 169 is similar to that cited in present claims 131-138, respectively.
171:	Support is found in the text on page 18, lines 12-14, of the Specification.
172-174:	Support is found in the text on page 11, lines 10-15, of the Specification.
175-182:	The subject matter of claims 175 to 182 is similar to that cited in present claims 140 to 147, respectively.
183:	Support is found in the text on page 17, lines 7-9, of the Specification.
184:	Support is found in the text on page 17, lines 9-11, of the Specification.
185:	Support is found in the text on page 17, lines 16-18, of the Specification.
186:	Support is found in the text, page 17, lines 16-18, of the Specification.

To the extent that the amendments avoid the prior art or for other reasons related to patentability, competitors are warned that the amendments are not intended to and do not limit the scope of equivalents which may be asserted on subject matter outside the literal scope of any patented claims but not anticipated or rendered obvious by the prior art or otherwise unpatentable to applicants. Applicants reserve the right to file one or more continuing and/or divisional applications directed to any subject matter disclosed in the application which has been canceled by any of the above amendments.

The Rejection under 35 U.S.C. § 103

The rejection of the previous claims under 35 U.S.C. § 103, as being obvious over Guerin (Intnl. J. Andrology) is respectfully traversed.

As previously discussed, Guerin relates to compositions and methods for male contraception utilizing hormones which are administered daily. Guerin teaches only the following three hormone combinations and routes for administration (see the Summary, p. 187):

a) daily MPA progestin orally combined with daily testosterone or 5α-dihydrotestosterone percutaneously;

b) daily norethisterone acetate (5 mg twice daily or 10 mg once daily) orally combined with daily testosterone percutaneously; and

c) daily norethisterone acetate combined with testosterone undecanoate, both administered orally.

Guerin thus relates only to two specific manners of oral administration of a norethisterone derivative progestogen in combination with oral or percutaneous administration of an androgen. Guerin fails to teach methods or compositions whereby a norethisterone derivative is in a non-oral form or is administered non-orally. Guerin also fails to teach methods or compositions providing for an extended contraception effect, e.g., at least 4 weeks, upon a single administration.

Contrary to suggesting non-orally administrable compositions or methods, Guerin suggests that their methods for oral administration are desired over non-oral or sustained activity methods. Guerin mentions that conventional methods of male contraception include the combination treatment with a progestagen (such as medroxyprogesterone acetate (MPA)) and an androgen (mainly testosterone enanthate) (see page 188, lines 1-3). The reference

further mentions that in conventional therapies both steroid classes are generally administered by intramuscular injections, with high initial doses followed by maintenance doses injected monthly or biweekly (page 188, lines 1-6). Guerin states that these known injection therapies with steroids are disadvantageous for two reasons, i.e., because they are allegedly not well accepted by the subjects and, additionally, allegedly the plasma levels of steroids are not constant, in particular, the androgen levels are decreased rapidly after a short period of increase following injection (page 188, lines 10-14).

Contrary to suggesting modification of its methods to provide a norethisterone derivative and androgen in non-oral, sustained-delivery form, the objectives of Guerin include avoiding what they considered the disadvantages of injection-type administration methods and methods where a single administration is used to provide a prolonged effect. The overall teaching of Guerin is to effect male contraception by daily, non-oral administration methods, e.g., with norethisterone acetate and testosterone undecanoate (page 188, lines 18-23). Thus, Guerin does not suggest non-oral, such as injection, methods with longer intervals between the administration of the norethisterone derivative, such as intervals of not less than 4 weeks. Neither does the reference suggest using a composition in a form for such administration.

Because the reference fails to motivate one of ordinary skill in the art to modify its methods in a manner suggesting the claimed invention – in fact, it discourages such – it fails to establish a prima facie case of obviousness against the instant claims. The rejection under 35 U.S.C. § 103 should be withdrawn at least for this reason.

As further proof of the nonobviousness of applicants' invention, attached is an article by some of the present inventors published in J. Clinical Endocrinology & Metabolism. The article provides data supporting the advantage disclosed for the claimed method of providing

male contraception by suppressing spermatogenesis; see, e.g., page 18, lines 12-14, of the instant specification. The data surprisingly show that injection therapy including long intervals between administration of an embodiment of the invention using norethisterone enanthate and testosterone undecanoate results in significant suppression of the sperm count in males. As can be seen from the Kamischke article, the suppression of sperm count in males was investigated in a study including intramuscular injection in 6-weeks intervals of norethisterone enanthate in two different doses (treatment groups I and II). The injection regimen was compared with daily oral administration of norethisterone acetate (treatment group III). The acetate is the ester used in the Guerin disclosure. The dose of the mentioned norethisterone ester in treatment groups I, II and III, respectively, was 200 mg per 42 days, 400 mg per 42 days and 10 mg per day. All treatment groups further included the intramuscular injection of an androgen (testosterone undecanoate) also in 6-weeks intervals between injections. The study showed that azospermia was achieved in 13 of 14 men in treatment group I, in 11 of 12 men in treatment group II and in 12 of 14 men in treatment group III (see Kamischke et al, page 532, lines 25-32 and Fig 1). Thus, the concept of utilizing long intervals between the injection of a norethisterone ester, such as 6 weeks, resulted in effective suppression of the sperm counts. Specifically, it can be derived from the results that about 93% and 92% of the men in treatment groups I and II, respectively, achieved azospermia. Thus, the suppression of sperm count in group I was just as effective as in treatment group II although treatment group I included the halved dose of treatment group II, namely 200 mg per 42 days.

This effective azospermia achieved by the invention as shown in the above tests could not have been expected from the Guerin teachings. As noted above, Guerin's investigation was based, in part, on their expectation that long intervals between administration would lead

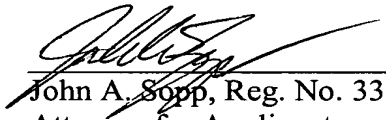
to an undesired secondary rise in sperm count. That the long interval method of applicants' invention was just as effective as daily administration was, thus, surprising in view of Guerin. It is urged that these unexpected advantages of the claimed invention further support the nonobviousness of the claimed invention.

For all of the above reasons, it is urged that Guerin fails to render the claimed invention obvious to one of ordinary skill in the art, i.e., neither the methods nor the compositions for carrying out such methods. The claimed invention contributes significantly to the art by providing an efficient and more acceptable regimen for male contraception including prolonged intervals between the non-oral administration of hormones. Thus, the rejection under 35 U.S.C. § 103 should be withdrawn.

It is submitted that the claims are in condition for allowance. However, the Examiner is kindly invited to contact the undersigned to discuss any unresolved matters.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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